

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L2	133	"35517"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2007/05/03 11:25
L3	3	"Re35517"	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2007/05/03 11:32
L4	84	allopregnanolone	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2007/05/03 11:32
L5	84	L4	US-PGPUB; USPAT; USOCR; EPO; JPO	OR	ON	2007/05/03 11:32

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NEWS 3 JAN 16 CA/Caplus Company Name Thesaurus enhanced and reloaded  
NEWS 4 JAN 16 IPC version 2007.01 thesaurus available on STN  
NEWS 5 JAN 16 WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data  
NEWS 6 JAN 22 CA/Caplus updated with revised CAS roles  
NEWS 7 JAN 22 CA/Caplus enhanced with patent applications from India  
NEWS 8 JAN 29 PHAR reloaded with new search and display fields  
NEWS 9 JAN 29 CAS Registry Number crossover limit increased to 300,000 in  
multiple databases  
NEWS 10 FEB 15 PATDPASPC enhanced with Drug Approval numbers  
NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records  
NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality  
NEWS 13 FEB 26 MEDLINE reloaded with enhancements  
NEWS 14 FEB 26 EMBASE enhanced with Clinical Trial Number field  
NEWS 15 FEB 26 TOXCENTER enhanced with reloaded MEDLINE  
NEWS 16 FEB 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements  
NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000  
to 300,000 in multiple databases  
NEWS 18 MAR 15 WPIDS/WPIX enhanced with new FRAGHITSTR display format  
NEWS 19 MAR 16 CASREACT coverage extended  
NEWS 20 MAR 20 MARPAT now updated daily  
NEWS 21 MAR 22 LWPI reloaded  
NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements  
NEWS 23 APR 02 JICST-EPLUS removed from database clusters and STN  
NEWS 24 APR 30 GENBANK reloaded and enhanced with Genome Project ID field  
NEWS 25 APR 30 CHEMCATS enhanced with 1.2 million new records  
NEWS 26 APR 30 CA/Caplus enhanced with 1870-1889 U.S. patent records  
NEWS 27 APR 30 INPADOC replaced by INPADOCDB on STN  
NEWS 28 MAY 01 New CAS web site launched

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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=> s allopregnanolone

L1 2857 ALLOPREGNANOLONE

=> s central nervous system or CNS

L2 880158 CENTRAL NERVOUS SYSTEM OR CNS

=> s L1 and (AY<2001 or PY<2001 or PRY<2001)

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L3 1071 L1 AND (AY<2001 OR PY<2001 OR PRY<2001)

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2 FILES SEARCHED...

'2001' NOT A VALID FIELD CODE

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L6 57 L5 AND (AY<2001 OR PY<2001 OR PRY<2001)

=> d 1-10 L6 ibib abs

L6 ANSWER 1 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:428567 CAPLUS  
DOCUMENT NUMBER: 140:400098  
TITLE: Neurosteroid regulation-based method of screening for  
nonsteroidal neuropsychiatric agents  
INVENTOR(S): Davis, John M.; Uzunov, Doncho P.  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S., 7 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
US 6740500	B1	20040525	US 2000-534831	20000323 <--
PRIORITY APPLN. INFO.:			US 2000-534831	20000323 <--
AB	A method of screening for nonsteroidal neuropsychiatric agents includes determining the ability of a candidate nonsteroidal agent to selectively regulate or alter the central nervous system content and/or bioavailability of an endogenous neuroactive steroid. In particular, the method includes determining the ability of the agent to selectively regulate a rate-limiting step in the biocontrol of the bioavailable amount of an endogenous neuroactive steroid, wherein the rate-limiting step may be either a step in biosynthesis of an endogenous neuroactive steroid, e.g. allopregnanolone, or a step in the biodegrdn. of such an endogenous neuroactive steroid. Alternatively, the method may include determining the ability of a candidate agent in selectively regulating the rate of reuptake of an endogenous neuroactive steroid by neurons or glial cells.			
REFERENCE COUNT:	27	THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L6 ANSWER 2 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2002:730545 CAPLUS  
DOCUMENT NUMBER: 137:242465  
TITLE: Method and compounds for use in the treatment of  
steroid induced states of the central  
nervous system  
INVENTOR(S): Backstrom, Torbjorn; Wang, Ming-De  
PATENT ASSIGNEE(S): Swed.  
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 37,869,  
abandoned.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
US 6455516	B1	20020924	US 1999-266035	19990311 <--
PRIORITY APPLN. INFO.:			US 1998-37869	B2 19980311 <--
OTHER SOURCE(S):	MARPAT 137:242465			
AB	The use of epiallopregnanolone (3 $\beta$ -hydroxy-5 $\alpha$ -pregnan-20-one) for the treatment of steroid induced mood disorders and CNS disorders is disclosed. Further, the use of epiallopregnanolone for the manufacture of pharmaceuticals is disclosed, together with an list of symptoms suitable for treatment with epiallopregnanolone.			
REFERENCE COUNT:	21	THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

L6 ANSWER 3 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2002:293431 CAPLUS

DOCUMENT NUMBER: 136:304454  
 TITLE: Methods for the treatment of a traumatic central nervous system injury  
 INVENTOR(S): Stein, Donald Gerald; Hoffman, Stuart Wayne  
 PATENT ASSIGNEE(S): Emory University, USA  
 SOURCE: PCT Int. Appl., 52 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030409	A2	20020418	WO 2001-US31705	20011010 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002072509	A1	20020613	US 2001-973375	20011009 <--
CA 2425650	A1	20020418	CA 2001-2425650	20011010 <--
AU 2002011612	A5	20020422	AU 2002-11612	20011010 <--
EP 1365752	A2	20031203	EP 2001-979677	20011010 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004532796	T	20041028	JP 2002-533852	20011010 <--
US 2005187188	A1	20050825	US 2005-85889	20050322 <--
PRIORITY APPLN. INFO.:				
			US 2000-239505P	P 20001011 <--
			US 2000-245798P	P 20001103 <--
			US 2001-973375	A 20011009
			WO 2001-US31705	W 20011010

AB The invention provides methods for conferring a neuroprotective effect on a population of cells in a subject following a traumatic injury to the central nervous system. Specifically, the methods of the invention provide for the administration of a progestin or progestin metabolite following a traumatic brain injury. The progestin or progestin metabolite is administered at therapeutically effective concns. that produce a neuroprotective effect (i.e., a decrease in the loss of neuronal activity) and reduces and/or prevents the various physiol. events leading to neurodegeneration, such as, cerebral edema and the immune/inflammatory response.

L6 ANSWER 4 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:93238 CAPLUS  
 DOCUMENT NUMBER: 134:141992  
 TITLE: Acute neuroactive steroid withdrawal in withdrawal seizure-prone and withdrawal seizure-resistant mice  
 AUTHOR(S): Reilly, M. T.; Crabbe, J. C.; Rustay, N. R.; Finn, D. A.  
 CORPORATE SOURCE: Portland Alcohol Research Center, Department of Behavioral Neuroscience, Oregon Health Sciences University, Portland, OR, 97201, USA  
 SOURCE: Pharmacology, Biochemistry and Behavior (2000), 67(4), 709-717  
 CODEN: PBBHAU; ISSN: 0091-3057  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal

LANGUAGE: English

AB Allopregnanolone (3 $\alpha$ -hydroxy-5 $\alpha$ -pregnan-20-one) is an endogenously derived metabolite of progesterone, and a potent pos. modulator of GABAA receptors. A withdrawal syndrome, characterized by central nervous system (CNS) hyperexcitability, has been demonstrated following abrupt discontinuation of high progesterone levels in rats, which was due in part to altered levels of allopregnanolone. The purpose of the present study was to determine if a single administration of pregnanolone or allopregnanolone could produce an acute withdrawal response in mice selected for susceptibility (Withdrawal Seizure-Prone, WSP) or resistance (Withdrawal Seizure-Resistant, WSR) to ethanol withdrawal convulsions. WSP mice administered 75 mg/kg pregnanolone showed a significant increase in handling-induced convulsion (HIC) scores over a 25-h testing period. In contrast, HIC scores in WSR mice were negligible after acute administration of 25, 50, 75, or 100 mg/kg pregnanolone. WSP mice also showed a similar increase in HIC after withdrawal from 75 mg/kg allopregnanolone. This effect was evident at both the 10-h and 25-h overall withdrawal severity assessment. These results demonstrate that neuroactive steroids can elicit an acute withdrawal response similar to that of other pos. modulators of GABAA receptors in WSP mice, supporting the notion that a common set of genes underlie acute and chronic withdrawal severity from multiple agents with depressant effects on the central nervous system.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:896030 CAPLUS

DOCUMENT NUMBER: 134:81034

TITLE: The effects of neurosteroids on picrotoxin-, bicuculline- and NMDA-induced seizures, and a hypnotic effect of ethanol

AUTHOR(S): Czlonkowska, A. I.; Krzascik, P. S.; Sienkiewicz-Jarosz, H.; Siemiatkowski, M.; Szyndler, J.; Bidzinski, A.; Plaznik, A.

CORPORATE SOURCE: Department of Experimental and Clinical Pharmacology, Medical Academy, Warsaw, 00-927, Pol.

SOURCE: Pharmacology, Biochemistry and Behavior (2000), 67(2), 345-353

CODEN: PBBHAU; ISSN: 0091-3057

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of i.p. (IP) or intracerebroventricularly (ICV) administered neurosteroids [allopregnanolone (AP); 5 $\beta$ -tetrahydrodeoxycorticosterone (5 $\beta$ -THDOC); dehydroepiandrosterone sulfate (DHEAS); pregnenolone sulfate (PS)] and their precursors [progesterone (PROG), pregnanediolone (PREG)] on N-methyl-D-aspartic acid (NMDA)-, picrotoxin (PTX)- and bicuculline (BIC)-induced seizures and ethanol-induced sleep were studied in mice. It was found that IP injections of (+)MK-801 most potently antagonized NMDA-, PTX- and BIC-induced seizures, as compared to diazepam (DZP), PROG and PREG. Both precursors of neurosteroids appeared only marginally active in the applied models of convulsions. ICV injections of AP selectively blocked PTX- and BIC-induced seizures, whereas 5 $\beta$ -THDOC and (+)MK-801 also antagonized NMDA-induced convulsions. ICV administered DHEAS induced seizures in a dose-dependent way. ICV injections of AP and midazolam shortened the latency and prolonged the duration of sleep induced by IP injections of ethanol (5.0 g/kg). On the contrary, DHEAS and PS significantly reduced the hypnotic-like effect of ethanol. The obtained results suggest that neurosteroids may modulate in an agonistic (AP, 5 $\beta$ -THDOC), or antagonistic way (PS, DHEAS), the GABAA receptor complex functions. Some of them (5 $\beta$ -THDOC) also interact with NMDA receptors. AP appeared to

be the most selectively acting compound, with its profile of action fully comparable to that of midazolam. AP also enhanced the hypnotic effect of ethanol, pointing out to the propensity to interact with centrally depressant agents. These findings, together with the possibility of conversion of some neurosteroids in the brain to other steroid hormones (testosterone, estradiol and aldosterone), indicate the limitations of their use for the treatment of neurol. and psychiatric disorders.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:734451 CAPLUS

DOCUMENT NUMBER: 133:329799

TITLE: Effects of estradiol and raloxifene analog on brain, adrenal and serum allopregnanolone content in fertile and ovariectomized female rats

AUTHOR(S): Genazzani, Andrea R.; Bernardi, Francesca; Stomati, Massimo; Monteleone, Patrizia; Luisi, Stefano; Rubino, Silvia; Farzati, Angelo; Casarosa, Elena; Luisi, Michele; Petraglia, Felice

CORPORATE SOURCE: Department of Reproductive Medicine and Child Development, Division of Obstetrics and Gynecology, University of Pisa, Pisa, I-56100, Italy

SOURCE: Neuroendocrinology (2000), 72(3), 162-170

CODEN: NUNDAJ; ISSN: 0028-3835

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Allopregnanolone is a neuroactive steroid synthesized in rat gonads, adrenal cortex, and central nervous system. It has been suggested that sex steroid hormones might influence allopregnanolone concns. but no clear data have ever been reported. The aim of the present study was to investigate the effects of administration of 17 $\beta$ -estradiol (17 $\beta$ -E2), the raloxifene analog LY-117018 or their combination on allopregnanolone levels in fertile and ovariectomized (OVX) rats. Thirteen groups of 12 Wistar female rats each received either 17 $\beta$ -E2 (0.1 or 1  $\mu$ g/day) or LY-117018 (25, 250, and 1250  $\mu$ g/day), or 17 $\beta$ -E2 1  $\mu$ g/day plus LY-117018: 25, 250, and 1250  $\mu$ g/day for 14 days. The rats were then sacrificed and allopregnanolone content was assessed in the hypothalamus, hippocampus, pituitary, adrenals, and serum. Ovariectomy determined a significant decrease in allopregnanolone content in the hypothalamus, hippocampus, pituitary, and serum, while increasing it in the adrenals ( $p < 0.01$ ). In OVX rats, the administration of either 17 $\beta$ -E2 or LY-117018 restored ovariectomy-induced allopregnanolone changes. The administration of LY-117018 in addition to 17 $\beta$ -E2 to OVX animals suppressed the increase in allopregnanolone levels determined by 17 $\beta$ -E2 in the hippocampus, hypothalamus, and pituitary, but not in the adrenals and serum. In fertile rats, the administration of LY-117018 reproduced the effects of ovariectomy. This study shows that the raloxifene analog LY-117018 has an estrogen-like action on the central nervous system of OVX rats when administered alone, while it acts as an antiestrogen in the presence of 17 $\beta$ -E2, both in OVX animals treated with 17 $\beta$ -E2 and in fertile rats. A different effect was observed in the adrenal glands. The mechanism of action of this compound has still to be clarified.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:587842 CAPLUS

DOCUMENT NUMBER: 133:291177

TITLE: Progesterone, progestagens and the central

nervous system

AUTHOR(S): Genazzani, A. R.; Stomati, M.; Morittu, A.; Bernardi, F.; Monteleone, P.; Casarosa, E.; Gallo, R.; Salvestroni, C.; Luisi, M.

CORPORATE SOURCE: Department of Reproductive Medicine and Child Development, Division of Gynecology and Obstetrics, University of Pisa, Pisa, 56100, Italy

SOURCE: Human Reproduction (2000), 15(Suppl. 1), 14-27

CODEN: HUREEE; ISSN: 0268-1161

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 57 refs.,. Estrogen, progestagens and androgens are able to modulate several brain functions. Receptors for gonadal steroids have been identified in several brain areas: amygdala, hippocampus, cortex, basal forebrain, cerebellum, locus ceruleus, midbrain rafe nuclei, glial cells, pituitary gland, hypothalamus and central gray matter. The mechanism of action of sex steroids at this level is similar to that observed in the peripheral target organs, including both genomic and non-genomic effects. The increased use of sex steroid hormone derivative therapies has lead to study of the biochem. and metabolic properties of the different progestin mols. available in hormonal therapies. In particular, exptl. and clin. studies focused the attention of researchers on interactions between estrogens and progestins in the neuroendocrine control of the brain functions and its clin. implications. Moreover, steroids are also synthesized de novo in the brain or may be derived from the conversion of blood-borne precursors, suggesting that the brain is also a source of steroids, named neurosteroids. Neurosteroids exert non-classical rapid actions as allosteric agonists of  $\gamma$ -aminobutyric acid receptor A (GABAA) and also modulate classic neurotransmitters in the brain. In addition, progesterone derivs., e.g., pregnanolone, and  $3\alpha$   $5\alpha$ -OH THP (allopregnanolone) are synthesized de novo by astrocytes and oligodendrocytes starting from cholesterol. Physiol. or pathol. modifications of the synthesis and release of neurosteroids play a relevant role in the control of brain function.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:521450 CAPLUS

DOCUMENT NUMBER: 133:188139

TITLE: Serum allopregnanolone levels in pregnant women: changes during pregnancy, at delivery, and in hypertensive patients

AUTHOR(S): Luisi, S.; Petraglia, F.; Benedetto, C.; Nappi, R. E.; Bernardi, F.; Fadalti, M.; Reis, F. M.; Luisi, M.; Genazzani, A. R.

CORPORATE SOURCE: Department of Reproductive Medicine and Child Development, Section of Gynecology and Obstetrics, University of Pisa, Pisa, Italy

SOURCE: Journal of Clinical Endocrinology and Metabolism (2000), 85(7), 2429-2433

CODEN: JCEMAZ; ISSN: 0021-972X

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Allopregnanolone is a neuroactive steroid measurable in peripheral circulation. The aim of the present study was to investigate the presence and the possible changes in serum allopregnanolone and progesterone levels in pregnant women during gestation, at delivery, and in patients with chronic hypertension, with or without superimposed preeclampsia. We also evaluated allopregnanolone in cord blood. Three groups of pregnant women were studied: (1) healthy controls followed



longitudinally throughout gestation (n = 14); (2) at vaginal or cesarean delivery (n = 66); and (3) with chronic hypertension (n = 12), with (n = 7) or without (n = 5) superimposed preeclampsia. Allopregnanolone and progesterone levels were measured in maternal and cord serum by RIA. In healthy pregnant women, serum allopregnanolone and progesterone levels progressively increased throughout gestation. Whereas no changes were found at vaginal delivery, serum allopregnanolone and progesterone levels were significantly lower at delivery by emergency cesarean section ( $P < 0.01$ ). Umbilical cord serum allopregnanolone and progesterone levels in emergency cesarean were significantly lower than those found at vaginal delivery ( $P < 0.01$ ). Patients with chronic hypertension, with or without superimposed severe preeclampsia, showed serum allopregnanolone levels significantly higher than those of healthy women at the same gestational age ( $P < 0.01$ ). In conclusion, maternal serum allopregnanolone levels increased during normal gestation were lower in women who underwent emergency cesarean and higher in patients with chronic hypertension, with or without preeclampsia. Because allopregnanolone is active on the central nervous system and in the control of systemic blood pressure, an involvement of this neurosteroid in the adaptive processes induced by pregnancy is suggested.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:398255 CAPLUS

DOCUMENT NUMBER: 133:115018

TITLE: Comparison of the neurophysiological effects of allopregnanolone and ethanol in rats

AUTHOR(S): Slawecki, C. J.; Walpole, T.; Purdy, R. H.; Ehlers, C. L.

CORPORATE SOURCE: Department of Neuropharmacology, The Scripps Research Institute, La Jolla, CA, 92037, USA

SOURCE: Psychopharmacology (Berlin) (2000), 149(4), 351-359

CODEN: PSCHDL; ISSN: 0033-3158

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rationale: The central nervous system actions of allopregnanolone (3 $\alpha$ -hydroxy-5 $\alpha$ -pregnan-20-one) and ethanol are at least partially mediated by modulation of  $\gamma$ -aminobutyric acid (GABA)-A receptors. Although ethanol and allopregnanolone have similar behavioral effects, their macro-electrophysiol. profiles have not been directly compared. Objective: The purpose of this study was to compare the effects of allopregnanolone and ethanol on the EEG (EEG) and event-related potentials (ERPs). Methods: Male Wistar rats were implanted with cortical and amygdalar electrodes. The rats were then administered allopregnanolone (0.0-10 mg/kg), ethanol (0.0-1.0 g/kg), or a combination of the two before recording. Results: Allopregnanolone and ethanol had similar effects on ERPs. When administered alone, both decreased cortical P1-N1 ERP amplitude by 25-50% and N1 amplitude in the amygdala by 75-80%. Combined administration of ethanol (0.50 g/kg) and allopregnanolone (5.0 mg/kg), doses which were ineffective alone, decreased N1 amplitude in the amygdala by 60%. Allopregnanolone and ethanol had dissimilar EEG effects. Allopregnanolone increased high frequency power in the cortex and amygdala by 25-30%. Ethanol decreased cortical and amygdalar power in the same high frequency bands by 25-45%. Allopregnanolone, but not ethanol, also shifted cortical frequency in the 32- to 50-Hz band. Combined administration of allopregnanolone and ethanol had no effect on EEG power but enhanced allopregnanolone's effect on cortical frequency. Conclusions: These data suggest that

allopregnanolone's macro-electrophysiol. profile resembles barbiturates and benzodiazepines more than ethanol. Further, the interactions of allopregnanolone and ethanol appear complex, with multiple effects observed (enhancement or reversal) depending on the neurophysiol. variable assessed.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:395968 CAPLUS

DOCUMENT NUMBER: 133:188346

TITLE: Characterisation of GABAA receptors in fetal, neonatal and adult ovine brain: region and age related changes and the effects of allopregnanolone

AUTHOR(S): Crossley, K. J.; Walker, D. W.; Beart, P. M.; Hirst, J. J.

CORPORATE SOURCE: Department of Physiology, Monash University, Clayton, 3168, Australia

SOURCE: Neuropharmacology (2000), 39(9), 1514-1522

CODEN: NEPHBW; ISSN: 0028-3908

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Progesterone metabolites acting via GABAA receptors suppress central nervous system (CNS)

activity. The aim of the present study was to examine binding characteristics of GABAA receptors in fetal, newborn and adult sheep brains using [35S]TBPS, and to determine the effects of allopregnanolone on this binding. Receptor affinity (KD) and d. (BMAX) in the brainstem were not different in fetal, newborn (1-2 days old) and adult brains. In the hypothalamus KD and BMAX increased significantly in the fetus between 85 and 128 days gestation, and were then similar to postnatal and adult values. In the frontal cortex KD and BMAX increased progressively between 85 days and term (.apprx.147 days gestation), and were then not different from postnatal and adult values. The Ki values for the GABAA receptor antagonist picrotoxin was similar at all ages. Allopregnanolone inhibited [35S]TBPS binding in the presence of 5  $\mu$ M GABA, but enhanced binding in the absence of GABA. These results show that (i), functional GABAA receptors are present in the fetal brain from at least 85 days gestation; (ii), 3 $\alpha$ -pregnane steroids modify receptor affinity in the late gestation fetal brain; and (iii) there are region-specific changes in GABAA receptor binding parameters. Steroid modulation of the GABAA receptor in the fetal brain is likely to influence fetal CNS activity in late gestation.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 11-15 ibib abs

L6 ANSWER 11 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:193022 CAPLUS

DOCUMENT NUMBER: 132:288956

TITLE: The neurosteroid allopregnanolone modulates oxytocin expression in the hypothalamic paraventricular nucleus

AUTHOR(S): Blyth, Brian J.; Hauger, Richard L.; Purdy, Robert H.; Amico, Janet A.

CORPORATE SOURCE: Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, 15261, USA

SOURCE: American Journal of Physiology (2000), 278(3, Pt. 2), R684-R691

CODEN: AJPHAP; ISSN: 0002-9513

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Virgin, ovariectomized rats exposed to 2 wk of sequential estradiol (E2) and progesterone (P) followed by P withdrawal have increased hypothalamic oxytocin (OT) mRNA and peptide levels relative to sham-treated animals. This increase is prevented if P is sustained. In the central nervous system, P is metabolized to the neurosteroid allopregnanolone (3 $\alpha$ -hydroxy-5 $\alpha$ -pregnan-20-one), which exerts effects by acting as a pos. allosteric modulator of GABAA receptor/Cl--channel complexes. In the present study, ovariectomized rats that received sequential E2 and P for 2 wk followed by P withdrawal were administered allopregnanolone at the time of P withdrawal. Hypothalamic and plasma allopregnanolone concns., serum E2 and P concns., and hypothalamic OT mRNA levels were measured at death. Steroid-induced increases in OT mRNA were attenuated in animals treated with allopregnanolone at the time of P withdrawal. The results suggest that allopregnanolone plays an important modulatory role in steroid-mediated increases in hypothalamic OT.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:189613 CAPLUS

DOCUMENT NUMBER: 132:303629

TITLE: In vivo evidences of early neurosteroid synthesis in the developing rat central nervous system and placenta

AUTHOR(S): Pomata, P. E.; Colman-Lerner, A. A.; Baranao, J. L.; Fiszman, M. L.

CORPORATE SOURCE: Laboratorio de Neurociencias, Centro de Investigaciones Medicas Albert Einstein Fundacion-CIMAE, Buenos Aires, 1416, Argent.

SOURCE: Developmental Brain Research (2000), 120(1), 83-86

CODEN: DBRRDB; ISSN: 0165-3806

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of the present study was to determine the developmental pattern of progesterone metabolism in rat brain and spinal cord from embryonic day 13 (E13) to the perinatal period. A marked decrease in the 5 $\alpha$ -reduction of progesterone in brain cortex was observed between E13 and postnatal day 5 (P5). Isopregnanolone was the predominant isomer in E13 in both cortex and spinal cord and its synthesis diminished gradually, while the concentration of allopregnanolone did not change significantly during development. The placental tissue was able to synthesize the 3 $\alpha$  and 3 $\beta$  isomers in E13, E16 and E19 embryos with allopregnanolone being the major metabolite in all the samples. We conclude that embryonic central nervous system tissues are able to synthesize neurosteroids at least from stage E13 and that they are developmentally regulated.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:145572 CAPLUS

DOCUMENT NUMBER: 132:275390

TITLE: Neuroactive steroid 3 $\alpha$ -hydroxy-5 $\alpha$ -pregnan-20-one modulates electrophysiological and behavioral actions of ethanol

AUTHOR(S): VanDoren, Margaret J.; Matthews, Douglas B.; Janis, Gregory C.; Grobin, A. Chistina; Devaud, Leslie L.; Morrow, A. Leslie

CORPORATE SOURCE: Departments of Psychiatry and Pharmacology, Bowles

Center for Alcohol Studies, and Curriculum in  
Neurobiology, University of North Carolina at Chapel  
Hill, Chapel Hill, NC, 27599-7178, USA  
SOURCE: Journal of Neuroscience (2000), 20(5),  
1982-1989  
CODEN: JNRSDS; ISSN: 0270-6474  
PUBLISHER: Society for Neuroscience  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Neuroactive steroids are synthesized de novo in brain, yet their physiol. significance remains elusive. We provide biochem., electrophysiol., and behavioral evidence that several specific actions of alc. (ethanol) are mediated by the neurosteroid 3 $\alpha$ -hydroxy-5 $\alpha$ -pregnan-20-one (3 $\alpha$ ,5 $\alpha$ -THP; allopregnanolone). Systemic alc. administration elevates 3 $\alpha$ ,5 $\alpha$ -THP levels in the cerebral cortex to pharmacol. relevant concns. The elevation of 3 $\alpha$ ,5 $\alpha$ -THP is dose- and time-dependent. Furthermore, there is a significant correlation between 3 $\alpha$ ,5 $\alpha$ -THP levels in cerebral cortex and the hypnotic effect of ethanol. Blockade of de novo biosynthesis of 5 $\alpha$ -reduced steroids using the 5 $\alpha$ -reductase inhibitor finasteride prevents several effects of ethanol. Pretreatment with finasteride causes no changes in baseline bicuculline-induced seizure threshold but reverses the anticonvulsant effect of ethanol. Finasteride pretreatment also reverses ethanol inhibition of spontaneous neural activity in medial septal/diagonal band of Broca neurons while having no direct effect on spontaneous firing rates. Thus, elevation of 3 $\alpha$ ,5 $\alpha$ -THP levels by acute ethanol administration represents a novel mechanism of ethanol action as well as an important modulatory role for neurosteroids in the CNS.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:746730 CAPLUS  
DOCUMENT NUMBER: 132:73803  
TITLE: Sex-Dependent Behavioral Effects of the Neurosteroid Allopregnanolone (3 $\alpha$ ,5 $\alpha$ -THP) in Neonatal and Adult Rats after Postnatal Stress  
AUTHOR(S): Zimmerberg, B.; Rackow, S. H.; George-Friedman, K. P.  
CORPORATE SOURCE: Bronfman Science Center, Department of Psychology, Williams College, Williamstown, MA, USA  
SOURCE: Pharmacology, Biochemistry and Behavior (1999), 64(4), 717-724  
CODEN: PBBHAU; ISSN: 0091-3057  
PUBLISHER: Elsevier Science Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The neuroactive steroid allopregnanolone (3 $\alpha$ -hydroxy-5 $\alpha$ -pregnan-20-one, 3 $\alpha$ ,5 $\alpha$ -THP) has been shown to be involved in the central nervous system's response to stress. This experiment investigated whether response to the neuroactive steroid allopregnanolone, a pos. modulator of the GABAA receptor, would be altered in neonatal or adult rats previously exposed to a chronic stressor-daily maternal separation during the first week of life. Subjects were then tested either as neonates or adults. In neonates, allopregnanolone decreased the number of ultrasonic vocalizations after brief maternal separation. Previously separated subjects vocalized less

and

were less active than controls, but were not more sensitive to allopregnanolone on either measure. In adulthood, subjects with a prior history of maternal separation had a greater grooming response to a novel environment after a 10-min cold water swim test than nonsepd. subjects. Allopregnanolone reduced grooming, but, again, there was no difference due to stress history. A significant effect of gender was

noted in the adult subjects-females were largely responsible for the effects reported. These results suggest that early maternal separation stress can produce an habituation response in neonates and a long-term sensitization response to later novel stress in adults. However, because the behavioral effects of allopregnanolone were not differentially influenced by this early stress history, the neuroactive steroid/GABAA receptor complex may not be the major mediator of these early stress sequela. Results indicating that females were more responsive to allopregnanolone than males are discussed in light of previous findings.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 15 OF 57 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:689631 CAPLUS

DOCUMENT NUMBER: 132:73727

TITLE: Neurosteroids: pharmacology and physiological implications in behavior

AUTHOR(S): Akwa, Yvette; Baulieu, Etienne-Emile

CORPORATE SOURCE: INSERM U488 Steroides, INSERM U488 Steroides et Systeme Nerveux, Le Kremlin-Bicetre, 94276, Fr.

SOURCE: Journal de la Societe de Biologie (1999), 193(3), 293-298

CODEN: JDSBFG

PUBLISHER: SGS

DOCUMENT TYPE: Journal; General Review

LANGUAGE: French

AB A review, with 27 refs. The term "neurosteroids" applies to those steroids that are both formed in the nervous system from sterol precursors, and accumulate in the nervous system, at least in part, independently of peripheral steroidogenic glands secretion. Neurosteroids, that are active on the central nervous system include, mainly, pregnenolone (PREG), dehydroepiandrosterone (DHEA) and their sulfate esters (PREG-S and DHEA-S), as well as the reduced metabolite of progesterone, 3 $\alpha$ ,5 $\alpha$ -TH PROG also called allopregnanolone. These neuroactive neurosteroids alter neuronal excitability by modulating the activity of several neurotransmitter receptors and thus can influence behavior. PREG-S decreases the sleeping time in rats anesthetized with a barbiturate, which is consistent with its antagonist action on the GABAA receptor (GABAA-R). Allopregnanolone is anxiolytic in rats tested in a conflict paradigm, through an interaction at a site specific for the benzodiazepine (BZ) receptor inverse agonist RO15-4513 and/or at the picrotoxinin site on GABAA-R. The contribution of the amygdala, a key region involved in the control of anxiety, is also demonstrated for the anxiolytic action of allopregnanolone. An anti-aggressive effect of DHEA can be observed in castrated male mice who become aggressive in the presence of lactating females. This inhibition of aggressiveness by DHEA is associated to a selective decrease in the brain of PREG-S, which may, in turn, trigger an increase of endogenous GABAergic tone. Finally, cognitive performances of aged rats tested in the Morris water maze and the Y-maze can be correlated with individual concns. of PREG-S in the hippocampus, i.e poor performance in both tasks with low levels of PREG-S. Remarkably, the memory deficits are significantly improved, albeit transiently, by an intra-hippocampal injection of PREG-S in impaired aged rats. Promnesiant PREG-S may then reinforce some neurotransmitter systems that can decline with age. This brief review provides evidence of the pharmacol. and physiol. correlates of neurosteroids involved in behavioral phenomena. However, neurobiol. mechanisms of behavioral effects of neurosteroids await further investigation.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d 50-55 ibib abs

L6 ANSWER 50 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2000:524165 BIOSIS  
DOCUMENT NUMBER: PREV200000524165  
TITLE: Allopregnanolone levels in children with pubertal  
disturbances.  
AUTHOR(S): Iughetti, L. [Reprint author]; Malagoli, C. [Reprint  
author]; Predieri, B. [Reprint author]; Luisi, M.; Forese,  
S. [Reprint author]; Bernasconi, S. [Reprint author]  
CORPORATE SOURCE: Department of Gynecological, Obstetrics and Pediatric  
Sciences, University of Modena and Reggio Emilia, Modena,  
Italy  
SOURCE: Journal of Endocrinological Investigation, (2000)  
Vol. 23, No. 6 Suppl., pp. 52. print.  
Meeting Info.: 23rd Meeting of Endocrinology. Pisa, Italy.  
June 28-30, 2000.  
CODEN: JEIND7. ISSN: 0391-4097.  
DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 6 Dec 2000  
Last Updated on STN: 11 Jan 2002

L6 ANSWER 51 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2000:442872 BIOSIS  
DOCUMENT NUMBER: PREV200000442872  
TITLE: Allopregnanolone levels in children with  
precocious puberty.  
AUTHOR(S): Iughetti, L. [Reprint author]; Predieri, F. [Reprint  
author]; Malagoli, C. [Reprint author]; Compagni, E.  
[Reprint author]; Petraglia, F.; Luisi, S.; Forese, S.  
[Reprint author]; Bernasconi, S. [Reprint author]  
CORPORATE SOURCE: Department of Gynecological, Obstetrics and Pediatric  
Sciences, University of Modena and Reggio Emilia, Modena,  
Italy  
SOURCE: Hormone Research (Basel), (July, 2000) Vol. 53,  
No. Suppl 2, pp. 93. print.  
Meeting Info.: 39th Annual Meeting of the European Society  
for Pediatric Endocrinology. Brussels, Belgium. September  
17-19, 2000.  
CODEN: HRMRA3. ISSN: 0301-0163.  
DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
LANGUAGE: English  
ENTRY DATE: Entered STN: 18 Oct 2000  
Last Updated on STN: 10 Jan 2002

L6 ANSWER 52 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2000:394063 BIOSIS  
DOCUMENT NUMBER: PREV200000394063  
TITLE: Neurosteroids and reproductive events: A new aspect of  
body-mind interplay for the steroids and the  
central nervous system.  
AUTHOR(S): Genazzani, A. R. [Reprint author]; Bernardi, F. [Reprint  
author]; Stomati, M. [Reprint author]; Luisi, S. [Reprint  
author]; Monteleone, P. [Reprint author]; Tonetti, A.  
[Reprint author]; Casarosa, E. [Reprint author]; Luisi, M.  
CORPORATE SOURCE: Department of Reproductive Medicine and Child Development,  
Section of Obstetrics and Gynecology, University of Pisa,

SOURCE: Pisa, Italy  
 Neuropsychopharmacology, (August, 2000) Vol. 23,  
 No. S2, pp. S40. print.  
 Meeting Info.: Second International Congress on Hormones,  
 Brain and Neuropsychopharmacology. Rhodes, Greece. July  
 15-19, 2000.  
 CODEN: NEROEW. ISSN: 0893-133X.

DOCUMENT TYPE: Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 13 Sep 2000  
 Last Updated on STN: 8 Jan 2002

L6 ANSWER 53 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on  
 STN

ACCESSION NUMBER: 2000:388954 BIOSIS  
 DOCUMENT NUMBER: PREV200000388954  
 TITLE: Central and peripheral progesterone metabolites.  
 AUTHOR(S): Backstrom, T. [Reprint author]; Bixo, M. [Reprint author];  
 Birzniece, V. [Reprint author]; Johansson, I.-M. [Reprint  
 author]; Olsson, T. [Reprint author]; Purdy, R. [Reprint  
 author]; Sundstrom-Poromaa, I. [Reprint author]; Wahlstrom,  
 G. [Reprint author]; Wang, M. [Reprint author]

CORPORATE SOURCE: Departments of Gynecology, Medicine and Pharmacology,  
 University of Umea, Umea, Sweden

SOURCE: Neuropsychopharmacology, (August, 2000) Vol. 23,  
 No. S2, pp. S40-S41. print.  
 Meeting Info.: Second International Congress on Hormones,  
 Brain and Neuropsychopharmacology. Rhodes, Greece. July  
 15-19, 2000.  
 CODEN: NEROEW. ISSN: 0893-133X.

DOCUMENT TYPE: Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 13 Sep 2000  
 Last Updated on STN: 8 Jan 2002

L6 ANSWER 54 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on  
 STN

ACCESSION NUMBER: 1999:46116 BIOSIS  
 DOCUMENT NUMBER: PREV199900046116  
 TITLE: Subunit dependent modulation of GABAA receptor function by  
 neuroactive steroids.

AUTHOR(S): Maitra, R.; Reynolds, J. N.

CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Queen's Univ., Kingston, ON K7L  
 3N6, Canada

SOURCE: Society for Neuroscience Abstracts, (1998) Vol.  
 24, No. 1-2, pp. 344. print.  
 Meeting Info.: 28th Annual Meeting of the Society for  
 Neuroscience, Part 1. Los Angeles, California, USA.  
 November 7-12, 1998. Society for Neuroscience.  
 ISSN: 0190-5295.

DOCUMENT TYPE: Conference; (Meeting)  
 Conference; Abstract; (Meeting Abstract)  
 Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 10 Feb 1999  
 Last Updated on STN: 10 Feb 1999

L6 ANSWER 55 OF 57 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on  
 STN

ACCESSION NUMBER: 1995:470085 BIOSIS  
 DOCUMENT NUMBER: PREV199598484385  
 TITLE: Brain allopregnanolone (AP) concentrations and

GABA-A receptor function in stressed rats.

AUTHOR(S): Barbaccia, M. L. [Reprint author]; Roscetti, G. [Reprint author]; Trabucchi, M. [Reprint author]; Concas, A.; Dazzi, L.; Purdy, R. H.; Biggio, G.

CORPORATE SOURCE: Dep. Exp. Med., Univ. Rome "Tor Vergata", 00133 Rome, Italy

SOURCE: Society for Neuroscience Abstracts, (1995) Vol. 21, No. 1-3, pp. 1345.

Meeting Info.: 25th Annual Meeting of the Society for Neuroscience. San Diego, California, USA. November 11-16, 1995.

ISSN: 0190-5295.

DOCUMENT TYPE: Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)  
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 1 Nov 1995  
Last Updated on STN: 1 Nov 1995